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FUNCTION IN CHILDREN IRA B. TAGER, M.D., M.P.H., SCOTT T. WEISS, M.D., M.S., ALVARO MUÑOZ, PH.D., BERNARD ROSNER, PH.D., AND FRANK E. SPEIZER, M.D.

LONGITUDINAL STUDY OF THE EFFECTS OF MATERNAL SMOKING ON PULMONARY

Abstract. We investigated the effects of maternal cigarette smoking on pulmonary function in a cohort of children and adolescents observed prospectively for seven years. A multivariate analysis revealed that after correction for

previous forced expiratory volume in one second (FEV₁), age, height, change in height, and cigarette smoking in the child or adolescent, maternal cigarette smoking significantly lowered the expected average annual increase in FEV, (P = 0.015). On the basis of this analysis, it is estimated that if two children have the same initial FEV1, age, height, increase in height, and personal cigarette-smoking

PREVIOUS studies have suggested 1-6 that maternal cigarette smoking influences the level of lung function in children. Most of these studies1-4 used analyses of cross-sectional data that left unanswered questions concerning the quantitative influence of maternal smoking on the development of lung function in children over time. As part of an ongoing study of childhood risk factors for the development of chronic obstructive airways disease, we investigated the effects of maternal eigarette smoking on pulmonary function in a cohort of children observed prospectively for seven years in East Boston, Mass.

METHODS

Selection and Screening of Sample

A 34 per cent random sample was selected from all children five to nine years of age who were enrolled in the public and parochial schools of East Boston, Mass., in September 1974. Between January and June 1975, using materials provided by the Division of Lung Diseases, National Heart; Lung, and Blood Institute interviewers visited the households of the index children and enumerated all residents. The residents of these households, plus the index children, constituted the initial study population. Initial examination of the subjects was conducted in a special neighborhood clinic between January and June 1975. Index subjects were visited in their homes during the school year (September to June); for six annual follow-up examinations; other family members were visited in their homes only for follow-up examinations 3 through 6. Follow-up interviews were conducted, whenever possible, within four calendar weeks of the date of the previous year's interview, usually between 2:00 p.m. and 8:00 p.m. For the initial and first two follow-up examinations, ewo interviewers were employed. All subsequent examinations were performed by only one of the two original interviewers.

Standardized questionnaires were used to obtain a history of respiratory symptoms and illnesses, as well as a smoking history and demographic data. At the initial examination and first two followup examinations, separate questionnaires were used for subjects

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tor award (HLI00740) from the Division of Lung Diseases, National Heart, Lung.

history, but the mother of one has smoked throughout the child's life whereas the mother of the other has not, the difference in the change in FEV, over-time in the exposed child, as compared with that in the unexposed child, will be approximately 28, 51, and 101 millafter one, two, and five years, respectively, or a reduction of 10.7, 9.5, and 7.0 per cent, respectively, in the expected increase. These results suggest that passive exposure to maternal cigarette smoke may have important effects on the development of pulmonary function in children. (N Engl J Med 1983; 309:599-703.)

under 10 years of age and for subjects 10 years or older. A common questionnaire was used for all subjects in the third through sixth follow-up examinations. The questions relating to chronic respira-tory symptoms were proposed for lung-program epidemiology studies by the Division of Lung Diseases, National Heart, Lung, and Blood Institute. For children aged 10 or younger, the parents answered all questions except those pertaining to the child's own smoking history; all other children answered all questions themselves. A smoking history was obtained directly from all children during pulmonary-function testing - a time when parents were not

Pulmonary-Function Testing

Forced vital capacity was measured while the subjects were in the sitting position, without nose clips, using an 8-liter water-filled, portable, recording spirometer (Survey Spirometer, Warren Collins, Braintree, Mass.), which was calibrated according to a regular schedule. Subjects were encouraged to perform the test until five acceptable tracings had been obtained or until it became evident. that they could not perform it adequately. For children in the preteen years, pulmonary-function tracings were considered acceptable if they were at least four seconds in duration (all other subjects were encouraged to blow for at least six seconds) and if the interviewer thought that a maximum effort had been made.

One-second forced expiratory volume (FEV1) and forced expirasory flow between the 25th and 75th per cent of forced vital capacity (FEF 25.75) were measured by standard techniques. When mean valwer were used; they were calculated as the mean of the best three of five tracings, as recommended by the Division of Lung Diseases, National Heart, Lung, and Blood Institute. All pulmonary-function measurements were corrected to body, temperature and pressure saturated with water vapor. Each subject's standing beight without shoes was measured to the nearest 1.3 cm. Mean function values were converted into per cent predicted values with the nomograms of Dickman et al." for subjects less than 25 and with those of Ferris et al. 10 for subjects 25 or older.

Definitions of Cigarette Smoking

At any given examination, subjects who were 20 or older were defined as never having smoked if they had never smoked or had smoked no more than one cigarette per day for more than one year or no more than 20 packs during their lifetime. "Current smokers" were defined as those who had smoked more than these amounts and who had been smoking within one month before the time of interview, for the initial examination, or for the entire year before and including the time of the interview, for the follow-up examinations. Examokers were defined as those who had stopped smoking more than one month before the interview. Subjects 19 or younger were considered never to have smoked if they had never smoked or

had smoked no more than one tigarette per week, as reported at each examination; otherwise, they were identified as "ever smokers" for that examination.

Methods of Data Analysis

Per cent predicted values for FEV₁ and FEF₂₂₋₇₃ for subjects 19 years or younger were divided into sex-specific five-year age groups (5 to 9, 10 to 14, and 15 to 19); per cent predicted values for subjects age 20 or older were divided into two sex-specific groups. Within each group, subjects were ranked, and the ranks were then converted to a cumulative frequency distribution. Each rank was then assigned a Z score from a table of areas under a standard normal curve. If Each score corresponds to the position of the subject's per cumulative frequency distribution; the mean score in each group was 0, with a variance of 1.

The mean Z score (FEV₁₁, FEF₂₂₋₇₃) for the first six years was

The mean Z score (FEV₁₁, FEF₂₃₋₇₃) for the first six years was calculated for each child as the average of all yearly values over this period. Because a variable number of annual observations was available for each child, the children were stratified according to the number of observations that were available to calculate their six-year mean values. (The median number of measurements was three, and the range was one to six. Sixty-two subjects, or 10.2 per cent, had aix measurements; only index subjects five to nine years of age at intake could have had as many as six. Forty per cent of the subjects had four or more.) The six-year mean Z scores for FEV₁ and FEF₂₃₋₇₃ were rank-ordered separately within each straum. For each lung-function measurement, the ranks were grouped into the lowest 20 per cent, the middle 60 per cent, and the highest 20 per cent of the ordered values. These groupings were then combined for all the strata. This procedure permits companisons of mean values in children who had different numbers of examinations.

To estimate the effect of parental smoking after controlling for the effects of the child's age, sex, initial height, increase in height, and personal smoking status, we used a Markov-type autoregressive model (Rosner B, et al.: unpublished data) similar to that proposed by Korn and Whittemore¹⁵ for a dichotomous outcome.

Chi-square analyses were performed with programs designed for programmable calculators by Rothman and Boice. 13

RESULTS

The study group consisted of 1156 white children from 404 families. At each examination, acceptable measurements of FEV₁ were obtained in more than 70 per cent of the available children (Table 1). The children in whom measurements of lung function were obtained were significantly more likely to be younger and female than those in whom such measurements were not obtained (Table 1). However, the children were comparable with regard to chronic respiratory

symptoms, mothers' education, mothers' smoking history, and type of home heating. In 75 per cent of the children in whom acceptable measurements of lung function were obtained in any given year, two or more such measurements were obtained over the first six examinations.

The percentage of children with mothers who were current smokers, as ascertained at either the initial or sixth examination, was highest among children with the lowest average levels of FEV fover the first six examinations (Fig. 1). The trend toward decreasing frequency of maternal smoking with increasing mean level of FEV fover the six examinations was significant (x1, trend = 11.1, P<0.001). Analysis of the FEF 25.75 levels gave results virtually identical to those for FEV. Similarly, analyses restricted to children who were cumulative "never smokers" at the sixth examination and to those with more than two pulmonary-function examinations gave results that were identical to those shown in Figure 1. No uniform trends were observed in comparisons of the smoking habits of fathers and the mean level of FEV1 or FEF 25.75 over the first six examinations.

The results of the autoregressive model relating change in FEV₁ over a one-year period to the mother's and the child's smoking status, after correcting for previous FEV₁, age, height, and one-year growth in height, are given in Table 2. The analysis, which is based on data from all seven examinations shows that the ollipping of mothers who were chirten cigarette smokers had significantly reduced similar increases in FEV₁ after correcting for all the other variables in the tables (P = 0.015). The total of the variables in FEV₁ at any point in time explained by the model was \$2.3 per cent.

The effects of the mother's and the child's smoking habits on the change in FE y in the child appeared to be additive; since no significant interaction was detected between these effects. Furthermore, neither the main effect of the father's smoking status nor the interaction of the father's and mother's smoking habits contributed significantly to the prediction of change in FEV₁ in the child.

The projected effects of the mother's smoking status on the annual rate of change of FEV₁ in a male child,

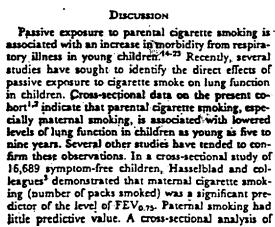
Table 1, Median Age and Age Range of Study Population, According to Sex, Number of Examinations, and Presence or Absence of Lung-Function Measurements.*

BLANDVATION MUNICIPA T	Дано-Румстви Мелициями		Forms	No Living-Function Meanneautr		TOTAL No. 1
	enis.	FRALL		- MI	-	
	median agr; range anches s	andan apr; saye	age; savge	medien age; sange	موسود زمون معاشده	
1	8 (443); 4-25	8 (409); 4-23	252	7 (169): 4-23	6 (135); 4-20	304
4	11 (381); 6-36	11 (336); 6-34	717	14 (60); 6-28	14 OIk 6-27	91
5	32 (345): 7-27	12 (313): 7-28	458	15 (91): 8-24	15 (39): 9-21	130
6	12 (332); 7-28	12 (301): 6-24	633	15 (106); 7-26	15 (72); 7-26	178

There is present or union of skilling

[•] The results of exemination 2 and 3 are not shown, since only dilibbraryed 5 to 9 years as the solution of the tohort wave model. As exemination 1 and 2, respectively, 23.4 per year and 36 per case of results inflores and long-function communities.

She of the shiften observed after the first executation had been some at the province paramination, where arbitrary were united at any province over product observer they were provinced.



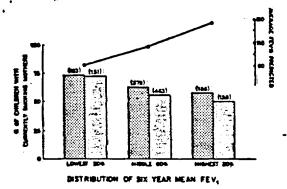


Figure 1. Percentage of Children with Mothers Who Were Current Cigarette Smokers at the Initial (Large Dots) and Sixth (Small-Dots) Examinations, According to the Distribution of Mean Age, Height, and Sex-Corrected FEV, over the First Six Examinations. "Lowest 20%," "middle 60%," and "highest 20%" refer to children with values in the bottom one fifth, middle three fifths, and upper one fifth, respectively, of the distribution of mean FEV, Numbers in parentheses indicate the number of children in each group. The three circles above the graph represent the average per cent predicted values of FEV, for the three groups. The results for male and female children were combined, since there was no significant difference between the sexes.

based on the model, are given in Table 3. The model predicted that over a two-year period, a nonsmoking male child with a currently smoking mother would accrue a 488-ml increase in FEV1, as compared with a 539-ml increase if the mother did not smoke. Over a five-year period, the child was predicted to accrue a 1335-ml increase in FEV1, as compared with a 1436anl increase if the mother did not smoke. If the child also smoked, then the accrued FEV, was predicted to be only 315 ml over two years and 993 ml over five years. Removal of the effect of maternal smoking from that of a child who smoked was predicted to result in an increase of 366 and 1094 ml of FEV; over two and five years, respectively, as compared with expected increases of 539 and 1436 ml.

A similar analysis was carried out for FEF25-75, but

Table 2, Regression Model Relating Change in FEV, over a One-Year Period to Mother's and Child's Smoking Status, after Correction for thitial FEV1, Age, Sex, Height, and Change in Height.

Vamidis	RECEIPMENT	STATEMED EARCH	P VALUE
Invercep t	-1.3390	9.0876	_
initial level of FEV ₁ (liners)	0.2389	0.0154	<0.001
Age (yr at time t)	-0.0099	8.0036	8.006
Sez (i = male)	0.0348	0.0112	0.002
Height (cm at since t)	0.0848	0.0053	<0.001
Change in height in 1 yr (cm)	0.0836	0.0107	<0.001
Child's smoking status ?	-0.0944	0.0278	≪0.001
Mother's smoking sums 1	-0.0278	8.0114	0.015

461 fewer person-years of observation were available than for the FEV, analysis, because current standards permit the calculation of FEV, from a tracing that does not give a valid measurement of FEF25-75-The effect of the mother's smoking status on FEF25-75 was in the same direction as its effect on FEV1, but the difference was not statistically significant after correction for the other variables in Table 2 ($\beta = 1-0.0366$, P = 0.174).

In a comparison of households in which the mother was or was not a current smoker, there was no significant difference (P = 0.173) in the percentage of mothers who had completed high school (used as a crude measure of socioeconomic status; 115 of 235, or 48.9 per cent, vs. 76 of 135, or 56.3 per cent, respectively, on the basis of information obtained at the initial examination). Furthermore, the use of gas stoves for cooking (used as a measure of potential indoor environmental confounding factors) was significantly more common in households with mothers who did not smoke than in those with mothers who did (28 of 133, or 21.1 per cent, vs. 20 of 163, or 12.3 per cent; $\chi_1^2 = 4.158$, P = 0.041; for households present at the end of the seventh examination, the first year these data were obtained).

Table 3: Effect of Child's and Mother's Cigarette-Smoking Habit on Expected Rate of Growth in FEV, over a Five-Year Period. Based on the Autoregressive Model.*

CHILD'S SHOEMS 1	MOTHER'S SHOEMS &	EXPECTED RATE OF GOOMTH IN FEV, (INC.)			
		erne I m	2 TB	47723 3 Th	
No	No	262	539	1436	
Yes	Nó	168 (64.1)	366 (67.9)	1094 (76.2)	
Niq	Yes	234 (89.3)	488 (90.5)	1335 (93.0)	
Yes	Yes	140 (53.4)	315 (58 4)	993 (69.2)	

anderlying risk predictor for obstructive airways disease in adult life. 22 Among the subjects in our analysis, socioeconomic status (assessed as maternal education) and exposure to gas cooking stoves did not appear to be responsible for the observed association between maternal smoking habit and rate of growth of lung

function.

4061 children in grades one through six4 also demonstrated an effect of parental cigarette smoking on the level of FEF23-75. As in our prior study, these authors found no effect on FEV, or forced vital capacity. The greatest effect was observed in female children with mothers who smoked. Initially, Speizer et al. found no effect of parental smoking²⁴; however, subsequent analysis has shown that children of mothers who smoke have significantly lower levels of FEV; than do children with mothers who do not smoke. In a study of children examined on two occasions over an average of 15 years, Higgins et all⁶ observed that pulmonary function was related to parental smoking history. Studies of adults in an industrial setting25 and in households²⁶ have shown that passive exposure to cigarette smoking has small effects on lung function; however, the health implications of some of these findings have been called into question.27

Several investigators have failed to establish any relation between parental eigarette smoking and lung function in children. In a cross-sectional study of children, Schilling and colleagues²⁸ found no significant effect of passive smoking on the levels of Vmax 50 and V_{max 25} (maximal flow when 50 and 75 per cent of the forced vital capacity had been expired), although they did observe that the levels were lowest in girls with mothers who smoked. However, when their analysis was restricted to children who had never smoked, the levels of Vmax 50 were significantly reduced in children with mothers who smoked. Since these authors used \hat{V}_{max} 50 and \hat{V}_{max} 25, which have a greater degree of variability than FEV, their study population may have been too small to detect an effect in all groups of children.29 Nonetheless, these data are not dissimilar to those of Schenker et al. 4 Dodge 30 failed to find any effect of parental smoking on changes in lung function in children studied over a four-year period, but this investigation used relatively insensitive analytic techniques. Finally, Lebowitz et al. 31 observed that after correction of children's lung function for the age and the body mass of their parents and for the children's body mass, there was no correlation between Z scores for lung function in children and parents. However, it is likely that this analysis was too insensitive to detect any effects of parental smoking, since the numbers were very small (the largest number of subjects in any group was 96).

Our longitudinal study detected a significant effect of maternal cigarette smoking on the change in a child's FEV, after controlling for the previous level of FEV1, age, sex, height, change in height, and the child's personal eigarette-smoking habit. The data in Table 3, which suggest that after five years, the lungs of nonsmoking children with mothers who smoke grow at only 93 per cent of the rate of growth in nonsmoking children with mothers who do not smoke, are certainly plausible in terms of the magnitude of the effect that one might predict for an environmental pollutant such as eigarette smoke. The size of the effect is consistent with that hypothesized to be sufficient as an

It is possible that the effect of maternal smoking at least in the postnatal period - is indirect. For example, there is an increased occurrence of acute respiratory illness in the children of mothers who smoke, as compared with the children of mothers who do not.14-23 Most of this effect has been observed during the first two years of life - a time when the lung may be particularly vulnerable to the long-term adverse consequences of such illnesses. 23,34 Thus, the observed effects of maternal cigarette smoking may be the consequence of structural changes that result directly from acute lower-respiratory illness early in childhood or indirectly from the long-term consequences of alterations in airway reactivity that may result from such illnesses. 34,35

Our study also shows that smoking habits in children have a substantial negative effect on the rate of increase in FEV₁. A similar negative effect was also observed in the analysis of FEF25-75 (P = 0.058). These results reinforce the already existing body of cross-sectional data suggesting that even a relatively low level of direct tobacco exposure in children and adolescents has measurable effects on pulmonary function.36-38

In summary, these data suggest that maternal smoking contributes to a reduction in the rate of development of lung function in children and, along with the child's own smoking habits, may be important in the development of chronic obstructive disease of the airways in adult life.

Addendien: Since submission of this manuscript, we have developed an algorithm to compute the parameter estimates given in Table 2, with adjustment for the intraclass correlation between children in the same bouseholds. The results of the analysis are essentially unchanged (mother's smoking = -0.0203, P = 0.03). The algorithm is available from the authors upon request.

We are indebted to Kay Mooradian and Mary Folsom, who obtained the data, and to Randy Whitfield and Vincent Carry, who provided the computer programming.

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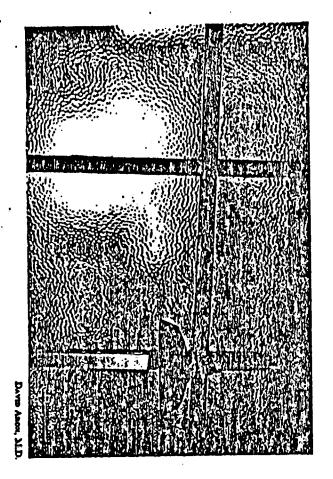
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ABSTRACT. We investigated the effects of maternal cigarette smoking on pulmonary function in a cohort of children and adolescents observed prospectively for seven years. A multivariate analysis revealed that after correction for previous forced expiratory volume in one second (FEV1), age, height, change in height, and cigarette smoking in the child or adolescent, maternal cigarette smoking significantly lowered the expected average annual increase in FEV1 (P=0.015). On the basis of this analysis, it is estimated that if two children havve the same initial FEV1, age, height, increase in height, and personal cigarette-smoking history, but the mother of one has smoked throughout the child's life whereas the mother of the other has not, the difference in the change in FEV1 over time in the exposed child, as compared with that in the unexposed child, will be approximately 28, 51, and 101 ml after one, two, and five years, respectively, or a reduction of 10.7, 9.5, and 7.0 percent, respectively, in the expected increase. These results suggest that passive exposure to maternal cigarette smoke may have important effects on the development of pulmonary function in children.